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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/518,610

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Ghanem Elias Ghanem

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MARSHALL, GERSTEIN & BORUN LLP  
233 SOUTH WACKER DRIVE  
6300 WILLIS TOWER  
CHICAGO, IL 60606-6357

EXAMINER

GUPTA, ANISH

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

08/19/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/518,610	<b>Applicant(s)</b> GHANEM ET AL.	
	<b>Examiner</b> ANISH GUPTA	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,6,11,16,18,20 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) 23 and 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2, 6, 16, 18, 20 and 25 is/are rejected.
- 7) ☒ Claim(s) 11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                        | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

1. Claims 23-24 submitted, 2-03-09, are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The newly added claims are drawn to method of treating cancer and method of treating other disorders selected from AIDs, parasitic disease etc. . . These claims corresponded to Group III in the restriction requirement mailed 10-4-07. In response to the restriction requirement, Applicants canceled all of the claims drawn to Groups II-VI. Examination was conducted on the claims corresponding to Group I.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 23-24 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. The amendment filed, 5/24/2010, is acknowledged. Claim 25 was added. Claims 1-2, 6, 11, 16, 18, 20 and 23-25 are pending in this application. Claims 23-24 have been withdrawn from consideration for the reasons set forth above.

3. All rejections made in the previous office action and not cited herein are hereby withdrawn.

### **Maintained Rejections**

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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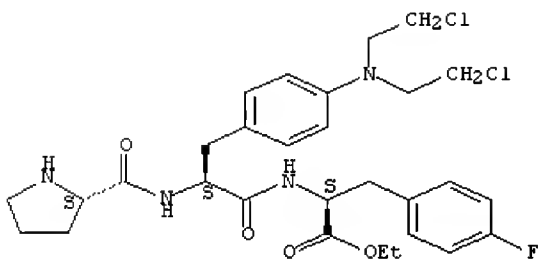
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2, 6, 16, 18, 20 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Lewensohn et al. (WO01/96367).

The claims are drawn to a tripeptide or tripeptide esters selected, where the tripeptide includes Pro-Phe-Phe and has a substituent at the not terminal amino acid moiety, with the proviso that said substituent is not  $-\text{N}(\text{CH}_2\text{-CH}_2\text{-Cl})_2$  in the meta position on the not terminal Pro-Phe-p-F-Phe.

The reference disclose the compound:



This compound is L-prolin-L-melfanyl-p-Fluorophenylalaline ethyl ester and is useful in treating malignant tumors (see claims). Note that the peptide sequence is Pro-phe-F-Phe, which meets the limitation of claims 21-22. The reference contains the substituent  $\text{N}(\text{CH}_2\text{-CH}_2\text{-Cl})_2$  in the central Phe residue. This compound meets the limitation of the claims because the instant specification states that page 3 that pharmacologically active groups include  $-\text{N}(\text{CH}_2\text{-CH}_2\text{-Cl})_2$  (see page 3, lines 15-17). Furthermore, example 1 disclose a similar compound, except the  $-\text{N}(\text{CH}_2\text{-CH}_2\text{-Cl})_2$  is in the para position, and states that “[t]his particular substituted tripeptide is bearing an alkylating group at the sarcolysine moiety. Said alkylating group is assumed to be the

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pharmacologically active part of the such substituted phenylalanine (*sic.*) moiety or - in other words- the drug loaded on the phenylalanine moiety." (see page 9, lines 16-24). Based this teaching, one can conclude that the even though -N(CH<sub>2</sub>-CH<sub>2</sub>-Cl)<sub>2</sub> is part of the sarcolysyl moiety, the drug is still loaded on the phenylalanine moiety. Thus, this meets the limitation of the claims.

Thus, the reference anticipates the claims.

### **Applicants Arguments**

Applicants argue that the specification makes a distinction between the term "drug," "reactive group," and "reactive site. Applicants assert that the compound recited in the prior art is distinguishable from the claimed invention because prior art recites a reactive group rather than a drug.

Applicants arguments have been fully considered but have not been found persuasive.

Applicants assert that the -N(CH<sub>2</sub>-CH<sub>2</sub>-Cl)<sub>2</sub> is a reactive group. However, there is sufficient basis to conclude that this group is a drug. First, the specification implies that this group is a drug. The specification states, on page 9, lines 16-24 "[t]his particular substituted tripeptide is bearing an alkylating group at the sarcolysine moiety. Said alkylating group is assumed to be the pharmacologically active part of the such substituted phenylalanine (*sic.*) moiety or - in other words- the drug loaded on the phenylalanine moiety." Note that the "alkylating group" corresponds to -N(CH<sub>2</sub>-CH<sub>2</sub>-Cl)<sub>2</sub>. Secondly, prior art discloses that the compound L-prolin-L-melphanyl-p-Fluorophenylalaline ethyl ester is useful in treating malignant tumors. The reference states that "[a]lkyating agents, such as drugs derived form nitrogen mustard, that is bis(2-chloroethyl)Amine derivates, are used as chemotherapeutic drugs in the treatment of a wide variety of neoplastic diseases." (see page 2, lines 3-8). Finally, the art recognizes that "nornitrogen mustard" injected into

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the bladder were effective against tumor growth. For example Wang et al. teaches and demonstrates the effectiveness of Cl-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>Cl against tumor cells (see abstract). Thus, based on the Applicants disclosure, the teachings of Lewensohn and the prior art as a whole, one of ordinary skill in the art would acknowledge that the -N(CH<sub>2</sub>-CH<sub>2</sub>-Cl)<sub>2</sub> moiety on the prior art peptide is not a reactive group but is a drug.

For this reason the rejection is maintained.

5. Claim 11 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. The reference of Wang et al. has been cited to refute Applicants contentions that -N(CH<sub>2</sub>-CH<sub>2</sub>-Cl)<sub>2</sub> is not a drug. The rejection under anticipation is made on the teachings of Lewensohn et al. (WO01/96367) alone. Thus, the application of Wang does not constitute a new ground of rejection.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on

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the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

/Anish Gupta/  
Primary Examiner, Art Unit 1654